PATENT
ATTORNEY DOCKET NO.: 059490-5025

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Ulrike SCHMID, et al.	)	
	)	
Application No.: 10/717,903	)	Group Art Unit:1642
	)	
Filed: November 21, 2003	)	Examiner: Unassigned
	)	
For: ANTI DIARRHOEA COMPOSITIONS	)	
	)	

MAIL STOP MISSING PARTS
Commissioner for Patent
Arlington, VA 22202

CLAIM FOR PRIORITY

Under the provisions of 35 U.S.C. §119, Applicants' hereby claim the benefit of the filing date of **European** Patent Application No. 02080021.5 filed November 27, 2002 for the above-identified United States Patent Application.

In support of Applicants' claim for priority, filed herewith is a certified copy of the European application.

Respectfully submitted,

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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

02080021.5

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

Anmeldung Nr:
Application no.: 02080021.5
Demande no:

Anmeldetag:
Date of filing: 27.11.02
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

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Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se referer à la description.)

Anti diarrhoea compositions

In Anspruch genommene Priorität(en) / Priority(ies) claimed /Priorité(s) revendiquée(s)
Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

A61K31/00

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR

ANTI DIARRHOEA COMPOSITIONS

In a number of areas such as in the pig breeding area but also in the medical area for humans, in particular for babies a known problem with the young mammels is that they easily suffer from diarrhoea. In the breeding industry an attempt to try to prevent and/or treat and/or cure diarrhoea (also named scour in the cattle industry) in the mammels sensitive for or suffering from it use was made of so called antimicrobial growth promotors (=AMGP's). Although some of these AMGP's give some relief they also possess a number of disadvantages such as that their use leads to the development of a resistance of the bacterial colonies responsible for the diarrhoea against the AMGP's. Therefore a number of National Health Organisations already decided that within a short period from now the use of these AMGP's will be prohibited. This created a great need to find replacers that are at least as effective as the AMGP's used so far, but for which the bacteria have not developed a resistance.

As the problems with diarrhoea are the most severe with weaning piglets and with babies the replacers should also be safe to use for these groups of mammels.

According to WO 02/056879 natural terpenes wherein the building block is a hydrocarbon isoprene can be used for this purpose. However these compounds have a number of disadvantages such as that they do not seem to reduce the incidence of number for veterinary control that is necessary for the young mammels fed with such components.

We studied whether we could find a useful replacer for the known AMGP's that are safe to use both for babies and for weaning piglets but also for other young mammels. Further these compounds should be effective and should not lead to a resistance within the bacteria responsible for the diarrhoea. Moreover these replacers should not have a negative effect on the growth (weight increase) of the young mammels when using them. Another requisite of these replacers being that they should not increase the incidence of number of veterinary controls necessary for the young mammels using the replacer during the weaning period.

The above studied has resulted in our novel invention. This invention concerns in the first instance a method for the prevention/curing/treatment of diarrhoea in mammels by adminstering the mammels an effective daily amount of a composition comprising as active component(s) phytosterols and /or pentacyclotriterpenes as present in shea oil or in fractions thereof. Preferably the young mammels are weaning piglets or babies.

It was found that the sterol and/or pentacyclotriterpene component(s) present in shea olein (olein being the liquid fraction that can be obtained by fractionation of shea oil either by solvent fractionation or by dry fractionation) or in concentrates thereof are very suitable as the active components However the active component also can be derivatives of these phytosterols or pentacyclotriterpenes. The most practical components being the phytosterols and/or pentacyclotriterpenes that have the natural composition of the shea sterols or shea pentacyclotriterpenes as present in shea olein. These components can comprise more than 50 wt % of 4,4-dimethylsterols or 4,4 dimethyl pentacyclotriterpenes selected from the group consisting of alpha-amyrin, beta-amyrin,

butyrospermol and lupeol. The sterols can however also be applied as free hydroxysterols (i.e. the acid groups such as acetic acid or cinnamic acid or fummaric acid which are attached to the sterols in shea have been removed therefrom e.g. by hydrolysis) or as fatty acid esters thereof (obtained by introduction of a fatty acid residue in the 2 position of the sterol or triterpene).

The effective amount can be determined by experimentation but in general this amount will be 0.5 to 30 gram / kg body weight of the mammel per day.

The active components can also be applied for the preparation of a food or a feed with the desired health property Therefore part of the invention is also a method for the preparation of a food or a feed product comprising carbohydrates and proteins wherein the food or feed product has anti-diarrhoea properties by the incorporation of an effective amount of phytosterols and /or pentacyclotrtiterpene derived from the sterols or triterpenes as present in shea oil as active component. The food or feed preferably comprises 0.001 to 4 wt % of the active component. A preference exists for the use of the natural components of shea olein i.e. the natural shea sterols, or shea pentacyclotriterpenes. In particular the active component will comprise at least 50 wt % of 4,4-dimethyl derivatives of shea sterols and/or of shea pentacyclotriterpenes selected from the group consisting of alpha-amyrin, beta-amyrin, butyrospermol and lupeol.

As a last embodiment of our invention we found novel animal feed comprising carbohydrates and proteins and 0.001 to 4 wt % of a shea olein comprising 2 to 12 wt % of (shea sterols plus shea pentacyclotriterpenes) or of a concentrate of shea sterols

and/or shea pentacyclotriterpenes comprising in total 12.5 to 80 wt% of these components.

EXAMPLES

Purpose

Evaluate the effect of supplementation with shea sterols on growth and post-weaning diarrhea of growing piglets.

The weaning of piglets is a very stressful event for these animals.

One day before the start of the experiment the pigs are weighed. The piglets are distributed over the different treatment groups with the aim to establish group equality in weight, sex. Piglets smaller then 5 kg or piglets with physical disturbances are excluded from the study.

At a mean age of 27 days the pigs are weaned and randomly assigned to the 3 experimental groups and are than treated for 35 days. Pigs are fed ad libitum. The first 14 days post weaning the pigs are fed a prestarter diet. Subsequently, the piglets are changed in a period of 3 days to a starter diet. Throughout the 35 day study period the food is supplemented with either:

1. without antimicrobial growth enhancers
2. with antimicrobial growth enhancers (AMGB: 40 ppm avilamycine)
3. with shea oleine (0.4%)

Piglets were weighed at the start of the experiment, at day 14 and at day 34.

Results

Growth figures

	no AMGB	AMGB	Shea extr.	
n=	220	220	190	
from weaning till 14 days post-weaning				
weight at weaning (kg)	7.7	7.7	7.7	
growth rate (g/day)	193	185	190	
food intake	0.25 [a]	0.23 [b]	0.25 [a]	p<0.001
food conversion	1.31	1.28	1.33	
EW-intake per day	0.28 [b]	0.26 [a]	0.28 [b]	p<0.001
EW-conversion	1.47	1.43	1.49	
from day 15 till day 34				
weight (kg)	10.7	10.5	10.5	
growth rate (g/day)	460	468	456	
food intake	0.72	0.72	0.72	
food conversion	1.56	1.55	1.57	
EW-intake per day	0.79	0.79	0.79	
EW-conversion	1.72	1.70	1.73	
from day 1 till day 34				
weight (kg)	20.8	20.9	20.5	
growth rate (g/day)	351	352	347	
food intake	0.53	0.52	0.52	
food conversion	1.51	1.49	1.51	
EW-intake per day	0.58	0.57	0.58	
EW-conversion	1.66	1.64	1.67	

The food intake of the piglets until 14 days post-weaning treated without AMGB's or with shea is increased compared to piglets on a diet supplemented with AMGB's

Incidence of diarrhoea (%)

	no AMGB	AMGB	Shea extr.	
First week post-weaning				
no diarrh.	80.6	81.2	80.8	
past. diarrh.	17.1	17.6	16.0	
watery diarrh.	2.3	1.2	3.2	
Second week post-weaning				
no diarrh.	87.5	90.3	91.2	p<0.1
past. diarrh.	12.5	9.5	8.8	
watery diarrh.	0.0	0.2	0.0	
Third week post-weaning				
no diarrh.	90.3	90.5	94.8	p<0.01
past. diarrh.	9.4	9.0	5	
watery diarrh.	0.3	0.5	0.2	
number of animals required treatment	26	23	10	

In the second week post-weaning the shea treated animals display trend towards a reduced incidence of diarrhea which reaches significance in week 3.

Conclusion

The shea extract reduces the incidence of diarrhea significantly in the third week post-weaning. Growth of the animals was similar in all groups. The number of animals that required veterinary treatment during the study was lowest in the shea treated animals (not significant)

Claims

1. Method for the prevention/curing/ treatment of diarrhoea in mammels by administering the mammels an effective daily amount of a composition comprising as active component(s) phytosterols and/or pentacyclotriterpenes as present in or derived from Shea oil.

2. Method according to claim 1 wherein the mammels are weaning piglets or babies.

3. Method according to claim 1 wherein the phytosterols and/or pentacyclotriterpenes have the natural composition of the shea sterols or shea pentacyclotriterpenes as present in shea olein

4. Method according to claim 3 wherein the shea sterols or pentacyclotriterpenes comprise more than 50 wt % of 4,4-dimethylsterols or 4,4 dimethyl pentacyclotriterpenes selected from the group consisting of alpha-amyrin, beta-amyrin, butyrospermol and lupeol.

5. Method according to claim 1 wherein the phytosterols are the free hydroxysterols.

6. Method according to claims 1 to 5 wherein the effective amount is 0.5 to 30 gram/kg body weight of mammel per day

7. Method according to claims 1 to 6 wherein the active phytosterols and/or pentacyclotriterpenes are administered as part of the food or feed for the mammel.

8. Method according to claim 7 wherein the food or the feed contains 0.001 to 4 wt % of the active component.

9. Method for the preparation of a food or a feed product comprising carbohydrates and proteins wherein the food or feed product has anti-diarrhoea or anti scouring properties by the incorporation of an effective amount of phytosterols and/or pentacyclotrtiterpenes as present in or derived from Shea oil as active component.

10. Method according to claim 11 wherein the food product or the feed product contains 0.001 to 4 wt % of the active component

11. Method according claims 9 or 10 wherein the active components are the natural shea sterols, and/or pentacyclotriterpenes.

12. Method according to claim 11 wherein the shea sterols and/or shea pentacyclotriterpenes comprise at least 50 wt % of 4,4-dimethyl derivatives of shea sterols and/or shea pentacyclotriterpenes selected from the group consisting of alpha-amyrin, beta-amyrin, butyrospermol and lupeol.

13. Animal feed comprising carbohydrates and proteins and 0.001 to 4 wt % of a shea olein comprising 2 to 12 wt % of (shea sterols plus shea pentacyclotriterpenes) or of a concentrate of shea sterols and/or shea pentacyclotriterpenes comprising in total 12.5 to 80 wt % of these components.

ABSTRACT

The invention concerns .a method for the prevention/curing/ treatment of diarrhoea in mammels by administering the mammels an effective daily amount of a composition comprising as active component(s) phytosterols and/or pentacyclotriterpenes as present in or derived from Shea oil as well as a method for the preparation of a food or a feed product comprising carbohydrates and proteins wherein the food or feed product has anti-diarrhoea or anti scouring properties by the incorporation of an effective amount of phytosterols and/or pentacyclotrtiterpenes as present in or derived from Shea oil as active component.